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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,000	09/26/2003	Anne Skaja Robinson	UOD-154US1	9773
66469	7590	01/09/2008		
RATNERPRESTIA P.O. BOX 1596 WILMINGTON, DE 19899			EXAMINER STEELE, AMBER D	
			ART UNIT	PAPER NUMBER
			1639	
			MAIL DATE	DELIVERY MODE
			01/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.		Applicant(s)	
	10/673,000		ROBINSON ET AL.	
	Examiner		Art Unit	
	Amber D. Steele		1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 13-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 19 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03/03/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 12, 2007 has been entered.

Status of the Claims

2. The amendment to the claims received on November 2, 2006 amended claims 3, 5, 8, 11, 14, and 17.

The amendment to the claims received on October 12, 2007 amended claims 1 and 7 and added new claims 19-20.

Claims 1-20 are currently pending.

Claims 1-12 and 19-20 are currently under consideration.

Election/Restrictions

3. Claims 1-6 are linking claims. Applicants elected Group I (Claims 7-12) in the reply filed on March 28, 2006 without traverse. Thus, claims 13-18 are withdrawn from consideration as being drawn to a non-elected invention.

Priority

4. The present application claims status as a divisional of 09/695,762 filed October 25, 2000, which claims benefit to provisional application 60/161,035 filed October 25, 1999.

Invention as Claimed

5. A method for recovering native protein from a sample comprising protein aggregates, said method comprising the steps of: (a) obtaining a sample comprising protein aggregates wherein said sample has been exposed to 3.5M urea or less; (b) subjecting the sample of step (a) to elevated hydrostatic pressure, whereby a portion of protein dissociates from said protein aggregates; c) returning the sample of step (b) to ambient pressure, whereby a portion of the dissociated protein refolds to native protein and variations thereof.

Withdrawn Objection

6. The objection to claims 2, 6, 9, and 12 as being dependent upon a rejected base claim is withdrawn in view of the new art of record and the 35 USC 112, first paragraph rejection (new matter). Thus, claims 2, 6, 9, and 12 are not free of the prior art.

Withdrawn Rejection

7. The rejection of claims 1, 3-5, 7, 8, 10, and 11 under 35 U.S.C. 102(b) as being anticipated by Gorovits et al. (*Biochemistry*, 4/28/1998, 37(17), pgs. 6132-6135) is withdrawn in view of the claim amendments received on October 12, 2007.

Claims Previously Indicated as Free of the Prior Art

8. The indicated allowability of claims 2, 6, 9, and 12 is withdrawn in view of the newly discovered reference(s) to Litt et al. U.S. Patent 6,635,469. Rejections based on the newly cited reference(s) follow.

New Rejections

Claim Rejections – 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-12 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection.

The amendment received on October 12, 2007 added the new limitation “wherein said sample has been exposed to 3.5M urea or less” in independent claims 1 and 7 and the new limitation “sample contains no urea” in new claims 19-20.

A. Applicants point to page 2, paragraph 29 of the published application (i.e. US2005/0020818); page 3, paragraph 37; pages 7-8; and Examples 7-8 (see excerpts and comments below) for support of the new limitation of independent claims 1 and 7.

Page 2, paragraph 29 excerpt: “One benefit of the present invention is that the use of the present invention can substantially or even entirely remove the need for urea or other denaturants.”

Page 3, paragraph 37 excerpt: “Until the present invention, however, high hydrostatic pressure has not been shown to reverse or inhibit protein aggregation so as to allow recovery of native protein, particularly in the substantial absence of denaturing agents such as urea.”

Pages 7-8 and Examples 7-8 do not recite “urea” or a concentration range for urea.

B. Applicants point to Examples 7-8; page 2, paragraph 14; and page 3, paragraph 37 of the published application (i.e. US2005/0020818; see excerpts and comments below) for support of the new claims 19-20.

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Examples 7-8 do not recite “urea” or a negative limitation stating that the samples contain no urea. 4

Page 2, paragraph 14 excerpt: “The invention also provides embodiment of such methods where the sample is substantially free of a denaturing agent selected from the group consisting of guanidine hydrochloride, guanidine thiocyanate, sodium dodecyl sulfate (SDS), and Urea.”

Page 3, paragraph 37 excerpt: “Until the present invention, however, high hydrostatic pressure has not been shown to reverse or inhibit protein aggregation so as to allow recovery of native protein, particularly in the substantial absence of denaturing agents such as urea.”

Therefore, the specification as originally filed does not have support for the limitation “wherein said sample has been exposed to 3.5M urea or less” or a sample that contains “no urea”. In addition, the specification as originally filed does not have support for any concentration range of urea (i.e. neither an open-ended range nor a closed range). Please refer to MPEP § 2163 (B); *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); and *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads). In addition, MPEP § 2163.05 states that “[t]he failure to meet the written description requirement of 35 U.S.C. 112, first paragraph, commonly arises when the claims are changed after filing to either broaden or narrow the breadth of the claim limitations, or to alter a numerical range limitation or to use claim language which is not synonymous with the terminology used in the original disclosure.” Furthermore, a negative limitation (i.e. no urea) requires support in the originally filed specification. The mere absence of a positive recitation is not basis for an exclusion (i.e. Examples 7-8). Additionally, a sample that is “substantially free” of urea is not considered a

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sample containing “no urea” because “substantially” implies that an amount (i.e. albeit a small or negligible amount) of the reagent is present in the sample. Please refer to MPEP § 2173.05(i).

Claim Rejections – 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-12 and 19-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Litt et al. U.S. Patent 6,635,469 (effective filing date of July 2, 1996).

For present claims 1 and 7, Litt et al. teach methods of recovering properly folded proteins from a sample comprising protein aggregates comprising (a) obtaining a sample comprising protein aggregates (i.e. including protein folding intermediates) without any urea or other chaotropic agents (i.e. 3.5M urea or less), (b) subjecting the sample to elevated hydrostatic pressure in order to partially dissociate proteins from aggregates, and (c) returning the sample to ambient pressure to allow refolding of the protein (please refer to the entire specification particularly columns 3-4, 6-12, and 15-20 and Examples). Litt et al. specifically teach that chaotropic agents are optional and that non-chaotropic agents may be utilized (please refer to the entire specification particularly column 4, lines 35-49; column 7, lines 27-40; column 8, lines 20-32; column 15, lines 51-67; column 16, lines 1-17; column 17, lines 45-67 and column 18, lines 1-31; column 19, lines 60-67; column 20, lines 1-5).

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For present claims 2, 6, 9, and 12, Litt et al. teach aggregates comprising inclusion bodies (please refer to the entire specification particularly column 17, lines 45-67 and column 18, lines 1-31).

For present claim 3, 5, 8, and 11, Litt et al. teach partial denaturing or reversible dissociation (please refer to the entire specification particularly column 9, lines 15-36; column 11, lines 46-56; column 15, lines 51-67; column 16, lines 1-17).

For present claims 4 and 10, Litt et al. teach that chaotropic agents are optional, non-chaotropic agents can be utilized, or temperature can be utilized instead (i.e. chaotropic agent in amount insufficient to denature protein at ambient pressure; please refer to the entire specification particularly column 4, lines 35-49; column 7, lines 27-40; column 8, lines 20-32; column 15, lines 51-67; column 16, lines 1-17; column 17, lines 45-67 and column 18, lines 1-31; column 19, lines 60-67; column 20, lines 1-5).

For present claims 19 and 20, Litt et al. teach urea as optional, utilizing temperature, utilizing non-chaotropic agents, utilizing chaotropic agents other than urea (i.e. no urea; please refer to the entire specification particularly column 4, lines 35-49; column 7, lines 27-40; column 8, lines 20-32; column 15, lines 51-67; column 16, lines 1-17; column 17, lines 45-67 and column 18, lines 1-31; column 19, lines 60-67; column 20, lines 1-5).

Therefore, the presently claimed method is anticipated by the teachings of Litt et al.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS

December 26, 2007

/Jon D. Epperson/
Primary Examiner, AU 1639